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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,590	01/15/2004	Dipak K. Dube	704690-3001	5121
21839	7590	04/18/2006	EXAMINER	
BUCHANAN INGERSOLL PC (INCLUDING BURNS, DOANE, SWECKER & MATHIS) POST OFFICE BOX 1404 ALEXANDRIA, VA 22313-1404			BRUSCA, JOHN S	
			ART UNIT	PAPER NUMBER
			1631	
DATE MAILED: 04/18/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/757,590	Applicant(s) DUBE ET AL.	
	Examiner John S. Brusca	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-13 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/15/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Priority

1. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. [1] as follows:

The first sentence of the specification was amended on 29 July 2005, but there is a typographical error in the immediate parent application number. It is apparent from the declaration filed 15 January 2004 that the applicants intended to claim priority as a continuation of Application No. 09/132231, however the first sentence of the specification was amended to cite priority to Application No. 09/132213. The applicants are requested to file an amendment to the specification correcting this error.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 06/887070, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Application No. 06/887070 fails to provide written description for a random sequence comprising an $x+y+z$ configuration as in the instant claims.

Specification

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR §§ 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the following reasons:

Several nucleotide sequences appear in the specification in figures 1, 3, and 6 that are not properly identified. Nucleotide sequences must be identified by sequence identification number. Furthermore, if said sequences do not appear in the sequence listing, a new listing including said sequences must be supplied. It is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP 2422.02). If said sequences consist of a portion of sequences already of record in the sequence listing, they may be identified in the specification using the existing SEQ ID No. accompanied by the position of the sequence on the already listed sequence.

Applicants are required to comply with all the requirements of 37 CFR §§ 1.821-1.825. Any response to this Office Action which fails to meet all of these requirements will be considered non-responsive. The nature of the sequences disclosed in the instant application has allowed an examination on the merits, the results of which are communicated below.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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5. Claims 3-13 recite the limitation "the expression vector" in line 3 of claim 3 and "the secreted protein" in line 11 of claim 3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 3-6, 12, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kauffman et al. (U.S. Patent No. 5,723,323) in view of Kaiser et al.

The claims are drawn to methods of isolating from selected cells a recombinant polynucleotide that comprises a random sequence with a non-random intervening sequence, in which the polynucleotide confers secretion of an encoded polypeptide to which it is operably linked. In some embodiments the sequence encodes a polypeptide of 13-36 amino acids, the cell

is *E. coli*, or eukaryotic, and the random polynucleotide sequences are no more than 24 nucleotides long.

Kauffman et al. shows in the abstract and throughout a method of screening a library of expression vectors comprising a random polynucleotide sequence that is expressed. Host cells comprising the expression vectors are screened for a desired property of a polypeptide encoded by the expression vectors. *E. coli* and eukaryotic host cells are discussed in column 2. Kauffman et al. shows a method of synthesizing polynucleotides with random sequences of approximately 630 bases in length which comprise a non-random intervening sequence by use of terminal transferase in column 5. Kauffman et al. does not show selection of cells that have conferred secretion to an operably linked encoded polypeptide, or use of random sequences no more than 24 nucleotides long, or random sequences that encode 13-36 amino acids.

Kaiser et al. shows in the abstract and throughout that random fragments of human genomic sequences operably linked to a gene can be selected for the ability to function as a signal peptide that confers secretion of linked encoded polypeptides. Kaiser et al. shows on page 312-313 selection of eukaryotic yeast cells for secretion of an invertase that is linked to a random sequence that serves as a signal peptide. The inserted randomized DNA sequences are on average 200 nucleotides long (page 313). Isolates that conferred secretion are shown in Figure 3, and were isolated with a surprisingly high frequency of about 20%. The length of the encoded random polypeptide range from as short as 20 amino acids to as long as 50 amino acids.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Kauffman by determining a property that is facilitation of secretion of an operably linked encoded polypeptide because Kaiser et al. shows

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that signal peptide characteristics may be studied by use of randomized sequences. It would have been further obvious to use of random sequences as short as 24 nucleotides long as a design choice to study the importance of a particular region of the signal peptide.

9. Claims 3 and 5-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kauffman et al. (U.S. Patent No. 5,723,323) in view of Kaiser et al. as applied to claims 3-6, 12, and 13 above, and further in view of Kadonga et al.

The claims are drawn to a method of selection of cells secreting a polypeptide linked to a randomized sequence, wherein the polypeptide is a beta lactamase and the selection is by use of ampicillin or tetracycline.

Kauffman et al. (U.S. Patent No. 5,723,323) in view of Kaiser et al. as applied to claims 3-6, 12, and 13 above does not show a method of selection of cells secreting a polypeptide linked to a randomized sequence, wherein the polypeptide is a beta lactamase and the selection is by use of ampicillin or tetracycline.

Kadonga et al. shows selection of mutants of beta lactamase signal peptide mutants by selection of expression vectors by use of tetracycline in figure 1. Kadonga et al. shows that mutants that are secreted may be distinguished by the level of ampicillin resistance of cells comprising the vector in Table II.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of assay of random sequences for the ability to confer secretion of operably linked polypeptides of Kauffman et al. (U.S. Patent No. 5,723,323) in view of Kaiser et al. as applied to claims 3-6, 12, and 13 above by use of ampicillin or tetracycline selection because Kadonga et al. shows that secreted beta lactamase can be distinguished by the

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level of ampicillin resistance, and the presence of an expression vector encoding the polypeptides of interest can be selected for by use of tetracycline.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Regarding use of the specification in obviousness-type double patenting rejections, the MPEP states in section 804:

When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. This does not mean that one is precluded from all use of the patent disclosure.

The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In *re Boylan*, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In *re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in *Vogel* recognized “that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim,” but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first “determine how much of the patent disclosure pertains to the invention claimed in the patent” because only “[t]his portion of the specification supports the patent claims and may be considered.” The court pointed out that “this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined.”

12. Claim 3 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,824,469. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claim of U.S. Patent No. 5,824,469 differs from instant claim 1 by being generic to the property of secretion

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that is claimed in instant claim 1. However, a screen for a property that is secretion is described in columns 4-5 of U.S. Patent No. 5,824,469.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(f) he did not himself invent the subject matter sought to be patented.

14. Claim 3 is rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

For the reasons discussed above, it is apparent that U.S. Patent No. 5,824,469 contains claimed subject matter in claims that is not patentably distinct from instant claim 3. Because the inventive entity of U.S. Patent No. 5,824,469 is different from the instant application, a rejection is appropriate under 35 U.S.C. 102(f). This rejection could be overcome by amendment of the appropriate claims so that the claims are patentably distinct, or by filing a declaration signed by the inventors of the rejected claimed subject matter stating the inventive entity for the commonly claimed subject matter is identical.

Conclusion

15. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of

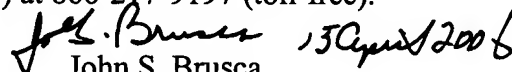
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the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


John S. Brusca
Primary Examiner
Art Unit 1631

jsb